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(54) **METHOD OF USING A CATHETER FOR DELIVERY OF ULTRASONIC ENERGY AND MEDICAMENT**

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(62) Division of application No. 08/878,463, filed on Jun. 18, 1997, now Pat. No. 5,997,497, which is a continuation of application No. 08/330,037, filed on Oct. 27, 1994, now abandoned.

(51) **Int. Cl.**[7] ................................................ **A61B 17/20**

(52) **U.S. Cl.** ......................... **604/22**; 604/500; 604/508; 606/128; 606/169; 601/2

(58) **Field of Search** ............................. 604/19–22, 500, 604/507, 508; 600/439; 606/128, 169; 601/2

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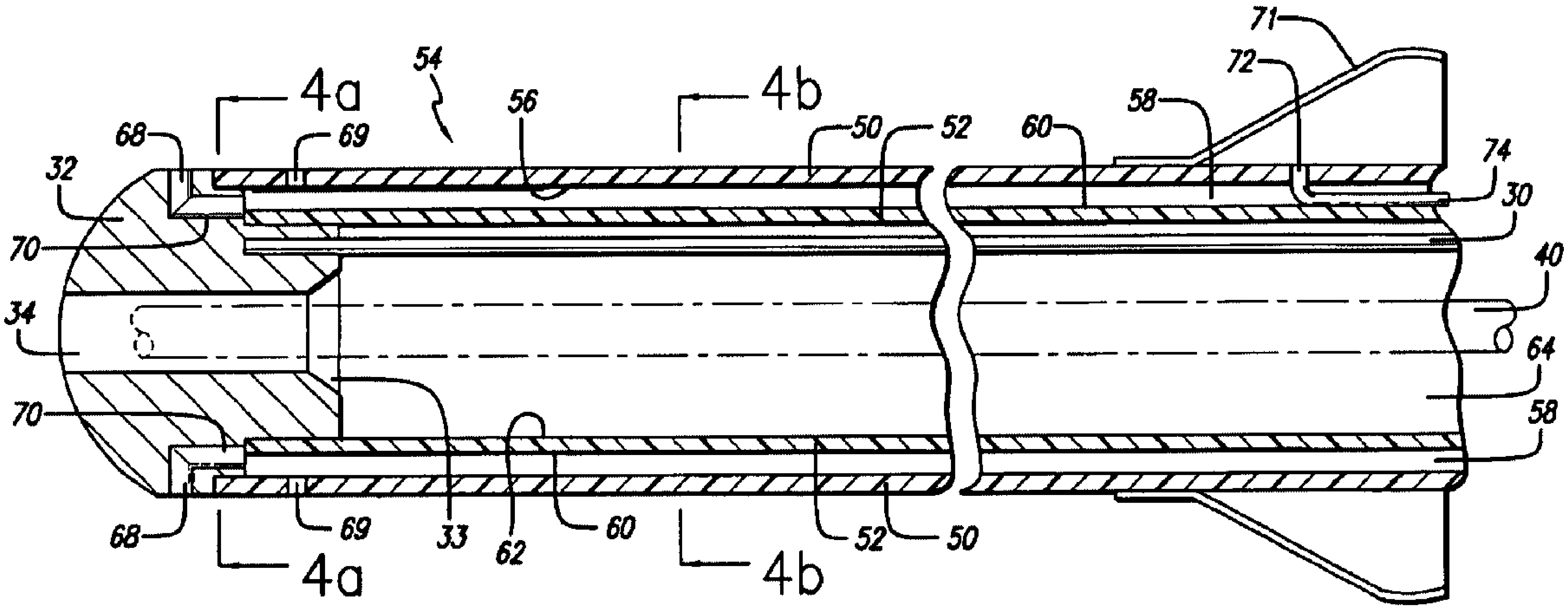
(57) **ABSTRACT**

An ultrasound delivery catheter equipped and configured for concurrent delivery of drugs or therapeutic agents. The catheter comprises an elongate pliable catheter body having an ultrasound delivery member or wire extending longitudinally therethrough. A drug/therapeutic agent infusion lumen also extends longitudinally through the body of the catheter and opens distally through one or more outflow apertures at or near the distal end of the catheter body. The drug/therapeutic agent outflow apertures are preferably positioned and configured to cause the drug or therapeutic agent to flow in direction(s) non-parallel to the longitudinal axis of the catheter. The delivery of ultrasound through the catheter, concurrent with infusion of drug or therapeutic agent therethrough, will cause the drug or therapeutic agent to be disseminated or dispersed by the ultrasonic vibration or movement at the distal end of the catheter.

**7 Claims, 3 Drawing Sheets**



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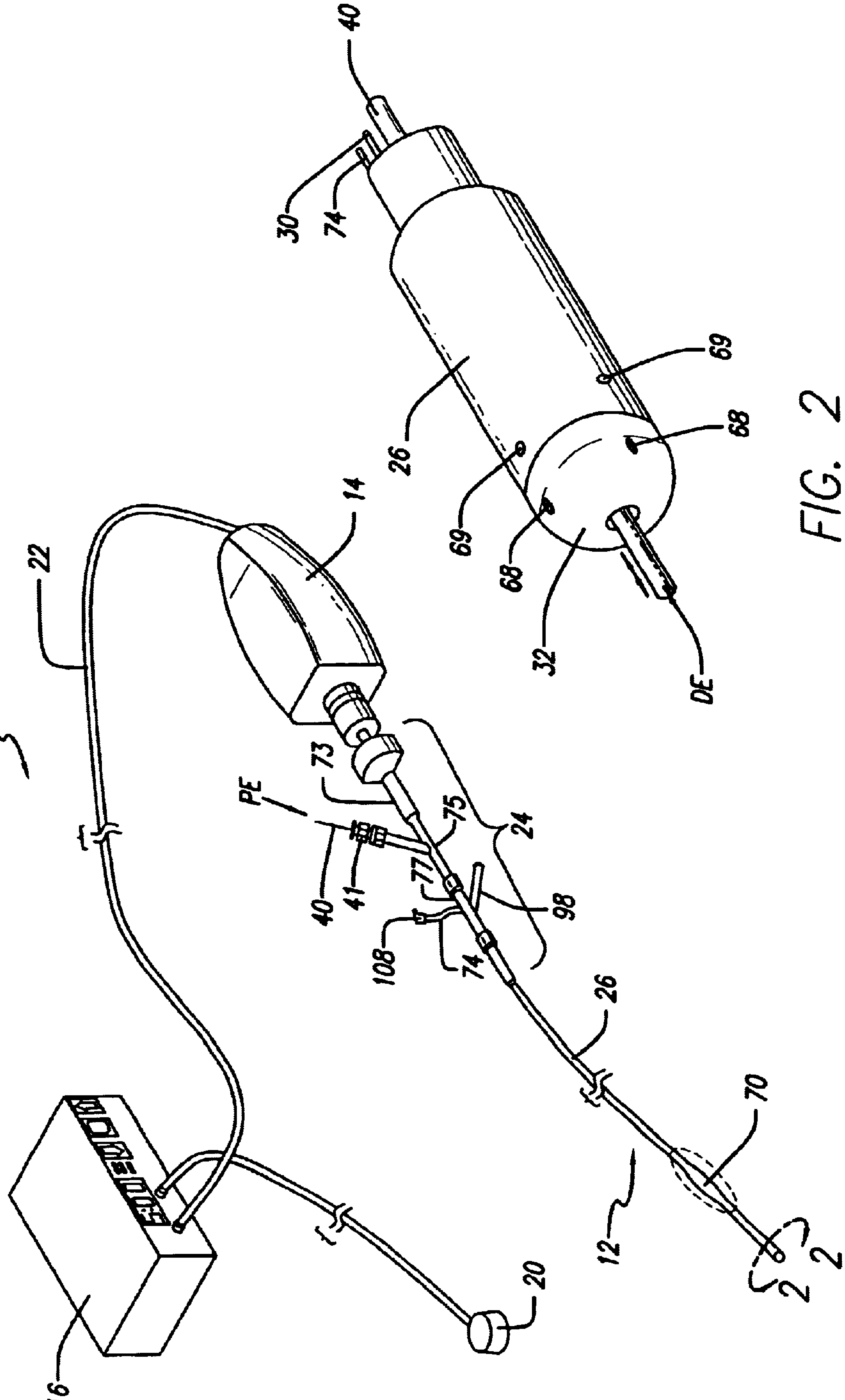



FIG. 1

FIG. 2

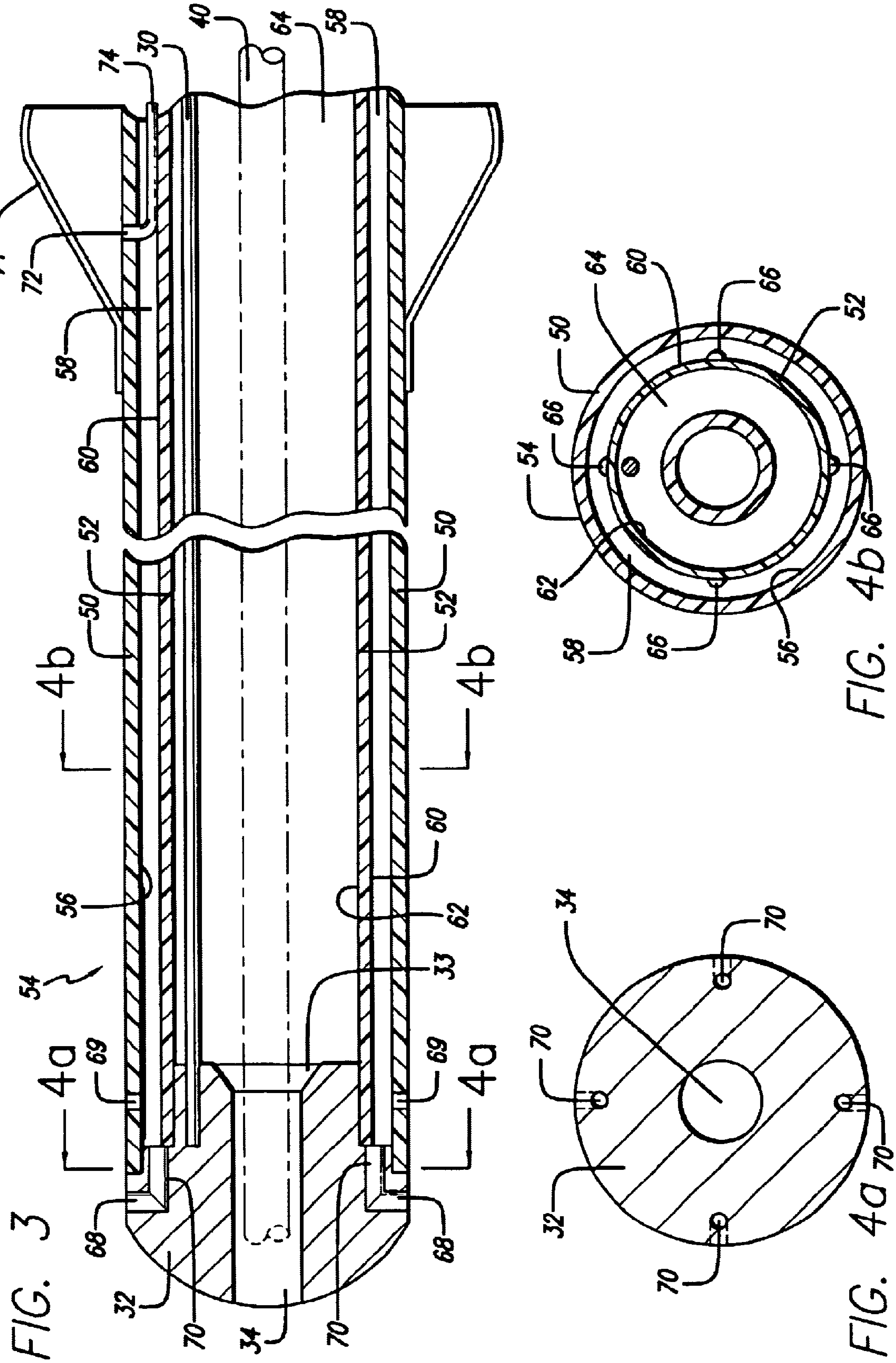
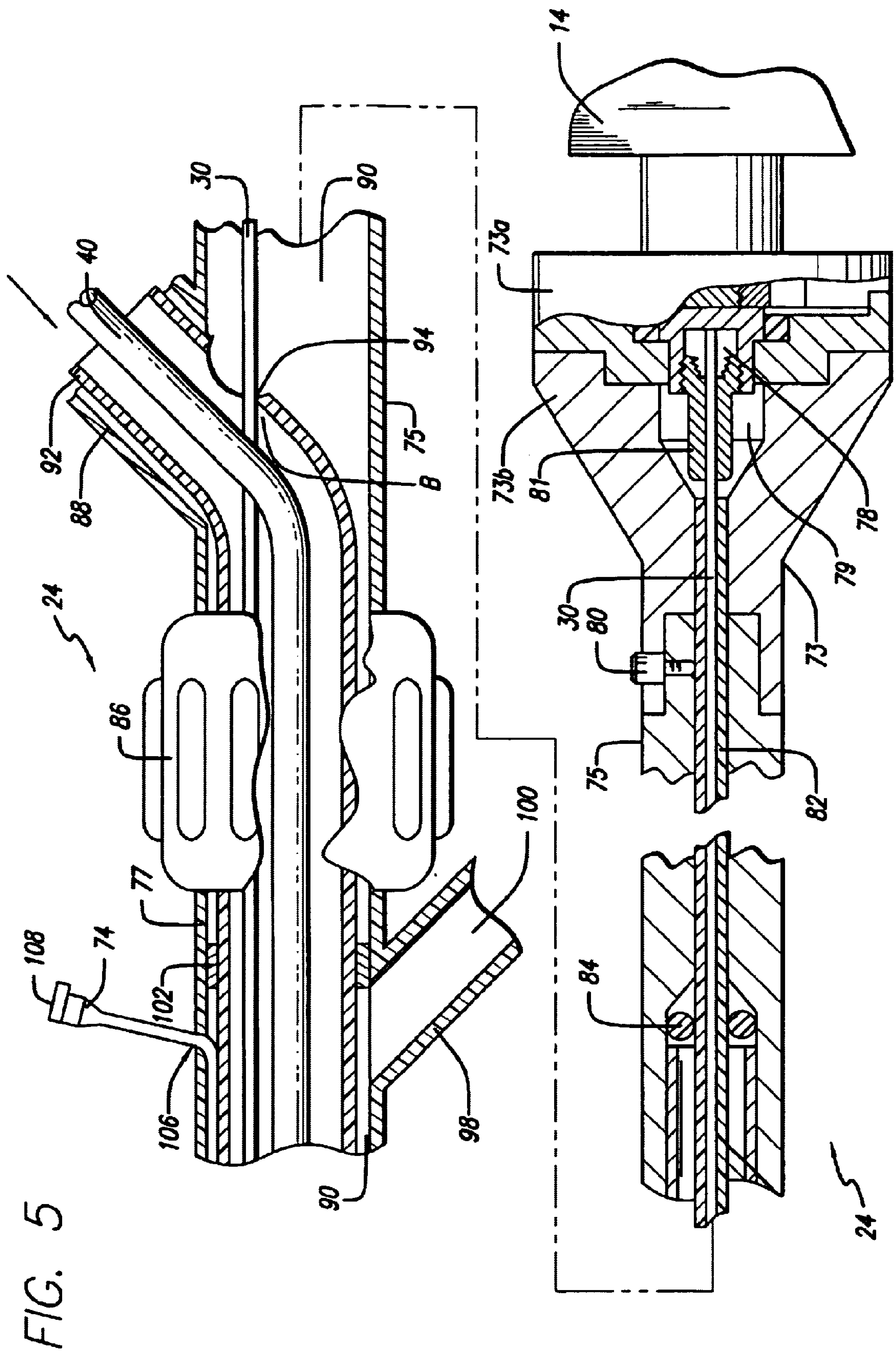



FIG. 3

FIG. 4a

FIG. 4b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24

FIG. 5

# METHOD OF USING A CATHETER FOR DELIVERY OF ULTRASONIC ENERGY AND MEDICAMENT

## RELATED APPLICATIONS

This is a division of application Ser. No. 08/878,463, filed Jun. 18, 1997 which is U.S. Pat. No. 5,997,497, which is a continuation of application Ser. No. 08/330,037, filed Oct. 27, 1994, abandoned.

## FIELD OF THE INVENTION

The present invention relates generally to medical equipment and more particularly to ultrasonic methods and devices which may be utilized to a) cardiovascular obstructions such as athroscloratic plaque or thrombus located in a mammalian blood vessel and b) to deliver an infusion of one or more therapeutic agents or drugs concurrently with ultrasonic energy so that the dissemination, dispersal, distribution, absorption, activity or duration of effected by the ultrasonic energy.

## BACKGROUND OF THE INVENTION

A number of ultrasonic devices have heretofore been proposed for use in ablating or removing obstructive material from anatomical structures, such as blood vessels. Examples of devices which purportedly utilize ultrasonic energy, alone or in conjunction with other treatment modalities, to remove obstructions from anatomical structures include those described in U.S. Pat. No. 3,433,226 (Boyd), U.S. Pat. No. 3,823,717 (Pohlman, et al.), U.S. Pat. No. 4,808,153 (Parisi), U.S. Pat. No. 4,936,281 (Stasz), U.S. Pat. No. 3,565,062 (Kuris), U.S. Pat. No. 4,924,863 (Sterzer), U.S. Pat. No. 4,870,953 (Don Michael, et al.), U.S. Pat. No. 4,920,954 (Alliger, et al.), and U.S. Pat. No. 5,100,423 (Fearnot) as well as other patent publications WO87-05739 (Cooper), WO89-06515 (Bernstein, et al.), WO90-0130 (Sonic Needle Corp.), EP316789 (Don Michael, et al.), DE3,821,836 (Schubert) and DE2,438,648 (Pohlman).

Ultrasound transmitting catheters have been utilized to successfully ablate various types of obstructions from blood vessels of humans and animals. Patients who are candidates for ultrasound ablation of vascular obstructions may also be candidates for treatment by various thrombolytic agents (i.e., blood clot dissolving agents) or other therapeutic agents or drugs.

Many types of therapeutic agents or drugs may be delivered by the ultrasonic catheter of the present invention. The types of agents or drugs which may be utilized in cardiovascular applications of the catheter include, but are not necessarily limited to, the following:

i. Thrombolytic Agents

Examples of thrombolytic agents utilized to dissolve thrombotic material include: streptokinase (Streptokinase for Infusion, Astra Pharmaceutical Products, Inc., Westboro, Mass., and Kabikinase™, Kabi Pharmacia, Piscataway, N.J.); urokinase (Abbokinase™, Abbott Laboratories, North Chicago, Ill.); and tissue plasminogen activator (TPA). Such agents are administered intravascularly following myocardial infarction or other cardio vascular events wherein a thrombus is suspected to be in formation or in existence.

ii. Anticoagulant Agents

Examples of anticoagulant agents utilized to prevent the subsequent formation of thrombus or blood clots include heparin (Heparin Sodium Injection, Wyeth-Ayerst Laboratories Philadelphia, Pa.).

In patients who are undergoing ultrasonic angioplasty procedures wherein a vascular obstruction is ablated by way of ultrasonic vibration, the administration of one or more therapeutic agents or drugs may be indicated before, during or after ultrasonic ablative procedure. Thus, it is desirable to design an ultrasonic ablation catheter through which various therapeutic agents or drugs may be delivered.

Additionally, it is desirable to design and devise new catheter devices for concurrently delivering a flow of liquid medicament along with ultrasonic vibration such that the distribution, delivery, absorption and/or efficacy of the medicament may be improved or enhanced by the ultrasonic vibration.

## SUMMARY OF THE INVENTION

The present invention provides improved ultrasound delivery catheters which incorporate means for infusing liquid medicaments (e.g., drugs or therapeutic agents) concurrently or in conjunction with the delivery of ultrasonic energy. The delivery of the ultrasonic energy through the catheter concurrently with the infusion of a liquid medicament will aid in rapidly dispersing, disseminating, distributing or atomizing the medicament. Additionally, it is postulated that the infusion of at least some types of liquid medicaments concurrently with the delivery of ultrasonic energy may result in improved or enhanced activity of the medicament due to a) improved absorption or passage of the medicament into the target tissue or matter and/or b) enhanced effectiveness of the medicament upon the target tissue or matter (e.g., thrombus) due to the concomitant action of the ultrasonic energy on the target tissue or matter.

Further in accordance with the invention, there are provided methods for treating various diseases or conditions by administering therapeutic agents or drugs concurrently or in conjunction with the delivery of ultrasonic energy.

Further objects and advantages of the invention will become apparent to those skilled in the art upon reading and understanding of the detailed description set forth herebelow, and consideration of the accompanying drawings.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a perspective view of an ultrasound/therapeutic agent delivery system of the present invention incorporating an ultrasound/therapeutic agent delivery catheter, an ultrasound transducer and an electronic signal generator.

FIG. **2** is an enlarged perspective view of the distal-most portion of the catheter shown in FIG. **1**.

FIG. **3** is a longitudinal sectional view of FIG. **2**.

FIG. **4***a* is a cross sectional view through line **4***a*—**4***a* of FIG. **3**.

FIG. **4***b* is a cross sectional view through line **4***b*—**4***b* of FIG. **3**.

FIG. **5** is a longitudinal sectional view of the proximal connector assembly of the catheter shown in FIG. **1**.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The following detailed description and the accompanying drawings are intended to describe and illustrate presently preferred embodiments of the invention only, and are not intended to limit the scope of the invention in any way. Indeed, the particular embodiments described herebelow are not the only embodiments in which the invention may be constructed and utilized.

FIG. **1** shows an ultrasound ablation/drug delivery system **10** of the present invention. The system **10** generally comprises an elongate ultrasound ablation/drug delivery catheter **12**, an ultrasound transducer **14** and an electrical signal generator **16**.

The signal generator **16** comprises a device operable to generate various wave-form electrical signals, such as the device available as Model UAG1110, Baxter Healthcare Corporation, Cardiovascular Group, Interventional Cardiology Division, Irvine, Calif. The preferred signal generator **16** incorporates a foot pedal on/off switch **20** for hand-free actuation/deactuation of the signal generator **16**. The signal generator **16** is connected to ultrasound transducer **14** by way of cable **22**. The ultrasound transducer **14** is operative to convert an electrical signal received from the signal generator **16**, to ultrasonic energy. One example of an ultrasound transducer **14** usable in the system **10** is that commercially available as model UAT-1000, Baxter Healthcare Corporation, Cardiovascular Group, Interventional Cardiology Division, Irvine, Calif.

The ultrasound catheter **12** of the present invention comprises an elongate flexible catheter body **26** having an elongate ultrasound transmission member or wire **30** which extends longitudinally therethrough. A proximal connector assembly **24** is positioned on the proximal end of the catheter body **26**. As shown in detail in FIG. **5**, and described more fully herebelow, the proximal connector assembly **24** includes a sonic connector apparatus **79** which facilitates connection of the proximal end of the ultrasound transmission member **30** to the ultrasound transducer **14** such that ultrasonic energy from the transducer **14** may be transmitted, in the distal direction, through the ultrasound transmission member **30** to the distal end of the catheter **12**.

The ultrasound transmission member **30** of the present invention may be formed of any suitable material capable of carrying ultrasonic energy from the proximal end of the catheter **12** to the distal end thereof. In particular, the presently preferred embodiment of the ultrasound transmission member **30** is formed of nickel-titanium alloy which exhibits superelastic properties within the temperature range under which the device is operated.

In particular, one presently preferred superelastic metal alloy of which the ultrasound transmission member **30** may be formed is nickel-titanium alloy consisting of 50.8 atomic percent nickel/balance titanium and is commercially available as Tinel™ BB from Raychem Corporation, Menlo Park, Calif.

The physical properties of the preferred 50.8 atomic percent nickel NiTi alloy are as follows:

Properties of NiTi Alloy
Having 50.8 At. % Nickel/Balance Titanium

| Property * | Units | Value |
|---|---|---|
| Superelastic Temperature Range | ° C. | 20 to 80 |
| Loading Plateau Stress (at 20° C.) | Mpa | 480 |
| Unloading Plateau Stress | Mpa | 135 |
| Permanent Set (at 20° C. after 8% strain) | % | 0.2 |
| Ultimate Tensile Strength (at 20° C.) | Mpa<br>Ksi | 1150<br>170 |

-continued

Properties of NiTi Alloy
Having 50.8 At. % Nickel/Balance Titanium

| Property * | Units | Value |
|---|---|---|
| Elongation at Failure | % | 10 |
| Melting Point | ° C. | 1350 |
| Density | g/cm<br>lbs/cu. Inch | 6.5<br>0.235 |

*Typical Values for Cold Worked and Shape Set Condition

Examples of superelastic metal alloys which are useable to form the ultrasound transmission member **22** of the present invention is described in detail in the U.S. Pat. No. 4,665,906 (Jervis); U.S. Pat. No. 4,565,589 (Harrison); U.S. Pat. No. 4,505,767 (Quin); and U.S. Pat. No. 4,337,090 (Harrison). The disclosures of U.S. Pat. Nos. 4,665,906; 4,565,589; 4,505,767; and 4,337,090 are expressly incorporated herein by reference insofar as they describe the compositions, properties, chemistries, and behavior of specific metal alloys which are superelastic within the temperature range at which the ultrasound transmission member **22** of the present invention operate, any and all of which superelastic metal alloys may be useable to form the superelastic ultrasound transmission member **22**.

In the preferred embodiment, the ultrasound transmission member **30** may be specifically configured and constructed to provide desirable flexibility or bendability near the distal end of the catheter, while at the same time minimizing the likelihood of breakage or fracture of the ultrasound transmission member **24** during use. Bendability or pliability of the distal portion of the catheter is particularly desirable in coronary or cerebrovascular applications wherein the distal portion of the catheter is required to pass into small tortuous coronary or cerebral blood vessels.

In the particular embodiment shown, the catheter body **26** is constructed of an outer tube **50** and an inner tube **52**. The outer tube **50** has an outer surface **54** and an inner surface **56**. The outer surface **54** of the outer tube **50** forms the outer surface of the catheter body **26**, having an outer diameter $D_1$. The inner surface **56** of the outer tube **50** forms the inner or luminal surface of the outer tube lumen **58**, having an inner diameter $D_2$.

Inner tube **52** has an outer surface **60** and an inner surface **62**. The outer surface **60** of inner tube **52** has an outer diameter $D_3$. The inner surface **62** of the inner tube **52** forms the inner or luminal surface of the inner tube lumen **64**, and has an inner diameter $D_4$.

As shown, the inner tube **50** is coaxially positioned within the lumen **58** of the outer tube **50**. The outer diameter $D_3$ of the inner tube **52** is smaller than the inner diameter $D_2$ of the outer tube **50**, so as to provide a gap or space between the luminal surface **56** of the outer tube **50** and the outer surface **60** of the inner tube **52**, through which a liquid medicament may be infused.

The distal tip member **32** of the catheter **12** has a plurality of a hollow medicament passageways **70** bored or otherwise formed therein and opening through medicament outflow apertures **68** formed in the outer surface of the distal tip member **32**, to permit a liquid medicament being infused through the space between the inner tube **52** and the outer tube **50** to pass through the distal tip member **32** and out of the outflow apertures **68** formed therein.

Also, additional medicament outlet apertures **69** may be formed in the wall of the outer tube **50**, near the distal end thereof, such that some of the medicament being infused through the space between the inner tube **52** and outer tube **50** will flow outwardly through such apertures **69**. In the embodiment shown in FIGS. **2–3**, the additional medicament outlet apertures **69** are paired with, and located in spaced relation to the outflow apertures **68** formed in the distal tip members **32**. It will be appreciated, however, that various other arrangements and positionings of the respective medicament outlet apertures **68**, **69** may be utilized without departing from the intended purpose and function of the present invention. The size and numerousity of the medicament outlet apertures **68**, **69** may vary depending on the specific intended function of the catheter **12**, the volume or viscosity of the medicament intended to be infused, and/or the relative size of the therapeutic area to which the medicament is to be applied.

A guide wire passage bore **34** extends longitudinally through the distal tip member **32** and is provided with a chamfered or frustoconical proximal region **33** to facilitate distally directed entry of the distal tip of an advancing guidewire **40** into the proximal opening of the guide wire passage bore **34**.

An optional annular occlusion balloon **71** or inflatable collar may be mounted or formed on the outer surface **54** of the catheter body **26** at a location proximal to the medicament outflow apertures **68**, **69** to temporarily occlude blood flow through the blood vessel in which the catheter **12** is positioned. In the embodiment shown the balloon **71** comprises a cylindrical elastic membrane mounted on the outer surface **54** of the outer tube **50**. A balloon inflation aperture **72** is formed in the side wall of the outer tube **50**, at a location beneath the balloon **71**. A small balloon inflation tube extends through the outer tube lumen **58**, outboard of the outer surface **60** of inner tube **52**, and is connected to the balloon inflation aperture **72** such that the balloon **71** may be inflated by injecting balloon inflation fluid through balloon inflation tube **74** and deflated by withdrawing balloon inflation fluid through tube **74**.

The proximal connector assembly **24**, as shown in FIGS. **1** and **5**, is mounted on the proximal end of the catheter body **26** and operates to connect the catheter **12** to an a) ultrasound transducer, b) a source of coolant fluid, c) a source of medicament for infusion and d) a source of balloon inflating fluid for inflating the annular occlusion balloon **71**. As shown, the preferred proximal connector assembly **24** generally comprises first **73**, second **75** and third **77** rigid body portions.

The first body portion **73** of the proximal connector assembly **24** is made up of two separate mated parts **73***a*, **73***b*, and forms the proximal-most end of the connector assembly **24**. A receiving depression (not shown) is formed in the proximal face of the first body portion **73**, to receive therein to facilitate connection of the transducer horn to the proximal end of the ultrasound transmission member **40**. The transmission of ultrasonic vibration from the transducer **14** into the ultrasound transmission member **40** is facilitated by a sonic connector apparatus **79** which is assembled and retained within the first body portion **73** of the proximal connector assembly **24**.

The sonic connector apparatus **79** comprises a compressible gripping ferrule **78** having a small central aperture formed therethrough, through which the ultrasound transmission member **40** passes, as shown. A frontal compression member **81** is threaded onto, and exerts inward pressure upon, the gripping ferrule **78** gripping ferrule **78** such that it frictionally engages the outer surface of the ultrasound transmission member **40** extending therethrough. This holds the ultrasound transmission member **40** in its desired longitudinal position. The proximal tip of the ultrasound transmission member **40** extends into the receiving depression (not shown) formed in the proximal face of the first portion **73** and is provided with a threaded sleeve (not shown) to threadably couple with the distal horn of an ultrasound transducer **14**. By such arrangement, ultrasonic energy may pass directly from the horn of the ultrasound transducer **14** into the ultrasound transmission member **40**, and will be carried thereby to the distal end of the catheter **12**.

The second body portion **75** of the proximal connector assembly **24** is connected to the first portion **73**, and secured thereto by way of set screw **80**. A hollow inner bore **90** extends longitudinally through the second and third body portions **75**, **77**, as shown. A lateral damping tube **82** is axially positioned around the portion of the ultrasound transmission member **30** which extends in the proximal direction from bore **90**, into the first body portion **73** of the connector assembly **24**. Such damping tube **82** is maintained in its substantially centered position within bore **90** by O-ring **84**. Such damping tube **82** serves to limit the amount of side to side or lateral movement that the ultrasound transmission member **40** may undergo in the region immediately proximal to the sonic connector apparatus **79**. The provision of such damping tube **82** serves to minimize the likelihood of breakage or fracture of the ultrasound transmission member **40** in the region immediately adjacent the point at which the ultrasound transmission member **40** is coupled to the ultrasound transducer **14**.

The third body portion **77** of the proximal connector assembly **24** is coupled to the proximal end of the catheter body **26** such that bore **90** is in fluid communication with the outer tube lumen **58**. A guide wire/coolant infusion side arm **88** extends laterally from the third portion **74** of the connector assembly **24**, and forms an inlet/outlet into the hollow inner bore **90** thereof. A curved guide wire diverter tube **92** is positioned within guide wire/coolant infusion side arm **88** and extends, in curved configuration, into the inner bore **90** of the proximal connector assembly **24**. The guide wire diverter tube **92** continues in the distal direction and is connected to the proximal end of the inner tube **52** of the catheter body **26** such that the lumen of the guidewire diverter tube **92** is continuous with the lumen of the inner tube **52** of the catheter. An aperture **94** is formed in the proximal side of the bend B formed in the guide wire diverter tube **92** and the ultrasound transmission member **40** passes directly into the lumen of the guide wire diverter tube **92**. The ultrasound transmission member **40** extends distally through the lumen of the diverter type **92** and through the lumen **64** of the inner tube **52** of the catheter body **26**, as shown. The angular bend B of the guidewire diverter tube **92** is configured to divert the advancing end of a guidewire **40** out of the guide wire/coolant infusion side arm **88**. By such configuration, the proximal end of a guide wire **40** may be inserted into the guidewire passage bore **34** and advanced proximally through the catheter body, and through the lumen **93** of the guide wire diverter tube **92** to a point where the proximal end of the guide wire will contact against the obtuse bend B, being thereby directed outwardly through the guide wire/coolant infusion sidearm **88**. Thus, the guide wire diverter tube **92** operates to guide or deflect the advancing proximal end of a guide wire **40** out of the guidewire/coolant infusion sidearm **88**, rather than allowing the guidewire to continue in the straight proximal direction through the bore **90** and into the first portion **73** of the proximal connector assembly **24**.

A guide wire gripping apparatus **41** such as that commercially available as product Nos. 1905017A and 1905014A from Medical Disposables International, West Conshocken, Pa., may be positioned on the guide wire side arm **88** to grip and hold the guide wire **40**, thereby preventing unwanted back and forth movement of the guide wire **40**. When it is desired to advance or retract the guide wire **40**, the guide wire gripping apparatus **41** may be loosened and the guide wire may be manipulated or removed as desired.

After the guide wire **40** has performed its required function, the guide wire gripping apparatus **41** may be loosened and the guide wire **40** may be extracted and removed. Thereafter, the guide wire gripping apparatus **41** may be removed from the guide wire/coolant infusion side arm **88**. A coolant infusion line may then be connected to guide wire/coolant infusion side arm **88** to provide a flow of coolant solution (e.g., sterile 0.9 percent NaCl solution) through the lumen of the guide wire diverter tube **92**, through the inner tube lumen **64** of catheter **12**, and out of the open guide wire passage bore **34** in the distal tip member **32** of the catheter **12**. Also, some coolant fluid will pass through the aperture **94** formed in the guide wire diverter tube **92** so as to fill the inner bore **90** of the proximal connector assembly **24**, in the region proximal to the point where the ultrasound transmission member **30** enters the guide wire diverter tube **92**. (FIG. **5**) Thus, the infusion of coolant fluid into the guide wire/coolant infusion side arm **88** will bath the ultra sound transmission member **30** and prevent overheating and potential thermal damage to the ultrasound transmission member **30** during operation.

The third portion **77** of the connector assembly **24** incorporates a forward extension attached by nut **86** and having a medicament infusion side arm **98** which extends laterally therefrom. The hollow bore **100** of the medicament infusion side arm **98** provides an opening into the inner bore **90** of the connector assembly **24**, outboard of the outer surface of the guide wire diverter tube **92**. As such, a medicament drug solution, such as a liquid therapeutic agent, or other liquid may be infused through medicament infusion side arm **98**, through the inner bore **90** of the connector assembly, through the outer tube lumen **58** of the catheter body **26** (outboard of the inner tube **52** disposed therewithin), and out of the medicament outflow apertures **68**, **69** at the distal end of the catheter **12**. An annular seal member **102** is mounted around the outer surface of the guide wire diverter tube **92**, at a location immediately proximal to the infusion side arm **98**, so as to form a seal between the outer surface of the guide wire diverter tube **92**, and the inner surface of the bore **90** of the proximal connector assembly **24**, thereby preventing the infused medicament or other liquid through medicament infusion side arm **98** from backflowing in the proximal direction through the connector assembly **24**. Thus, any drug solution therapeutic agent or other fluid infused through infusion side arm **98** will be caused to flow only in the distal direction, through the outer tube lumen **58** of the catheter **12** and out of medicament outflow apertures **68**, **69**.

Also, a balloon inflation tube escape aperture **106** is formed in the side wall of the **77** of the connector assembly **24**. The proximal end of the balloon inflation tube **74** is exteriorized through the aperture **106** and a fluid tight seal is formed therearound to prevent fluid from leaking from the bore **90** outwardly through aperture **106**. A Leur connector **108** is mounted on the proximal end of the balloon inflation tube **74** to facilitate attachment of a stop cock (not shown) balloon inflation and syringe (not shown) thereto.

## OPERATION OF THE PREFERRED EMBODIMENT

In accordance with standard clinical procedures, a guide wire **40** may be initially percutaneously inserted, and advanced through the vasculature to a point where the distal end DE of the guide wire **40** is positioned near or adjacent the intravascular obstruction to be ablated. Thereafter, the exteriorized proximal end PE of the guide wire may be directed inwardly through the guide wire passage bore **34** which extends through the distal tip member **32** of the catheter **12**, and the catheter **12** may then be advanced in the distal direction, over the guide wire **30**. As the inner tube lumen **64** advances distally over the preinserted guidewire **40**, the proximal end PE of the guidewire **40** it will enter the guidewire diverter tube **92** positioned within the proximal connector assembly **24**. As the proximal end PE of the guide wire **40** reaches the obtuse bend B of the guide wire diverter tube **92**, the proximal end PE of the guide wire **40** will be thereby deflected in the lateral direction, so as to pass outwardly through the guide-wire/coolant infusion side arm **88**. When the catheter **12** has been advanced to its desired operative position (i.e., when the distal tip member **32** of the catheter **12** is positioned adjacent or in contact with the thrombus or other obstruction to be ablated) the guide wire gripping apparatus **41** may be tightened to hold the catheter **12** in a fixed longitudinal position relative to the guide wire **40**. Alternatively, the guide wire **40** may be fully extracted and removed, through the guide wire side arm **88**.



After the catheter **12** has been advanced to its desired operative position, the ultrasound transducer **14** is connected or coupled, by way of the sonic connector apparatus **77**, to the proximal end of the ultrasound transmission member **30** such that ultrasonic vibration may be transmitted from the horn of the ultrasound transducer **14**, through the ultrasound transmission member **30**, and to the distal end of the catheter **12**.

After the guide wire **40** has been extracted and removed, the guide wire gripping apparatus **41** may be detached and removed from side arm **88** and an infusion tube may be connected to side arm **88** to infuse a flow of coolant fluid, such as sterile 0.9 percent saline solution, through guide wire/coolant infusion side arm **88**, through the inner tube lumen **64** of the catheter **12**, and out of the guide wire passage bore **34** of the distal tip member **32**. Such flow of infusion fluid will serve to cool the ultrasound transmission member **40** during operation thereof.

As the coolant fluid is being infused, the signal generator **16** is actuated by depression of on/off foot pedal **20**, thereby sending an electrical signal from the signal generator **16** to ultrasound transducer **14**. The ultrasound transducer **14** then converts the received electrical signal into ultrasonic energy and such ultrasonic energy is then transmitted through the ultrasound transmission member **40** to the distal tip member **32** of the catheter **12**. The vibrating distal tip member **32**, being in abutment with and attached to the distal end of the catheter body, will cause the adjacent distal portion of the catheter body **26** to vibrate as well. As the distal portion of the catheter **12** vibrates, the operator may move the catheter **12** back and forth to cause the distal end of the catheter to traverse the region of the thrombus or occlusion to be ablated such that the ultrasonic vibration of the distal tip member **32** and adjacent distal portion of the catheter body **26** will cause ultrasonic ablation of the thrombus or other obstructive matter.

Concurrent with the delivery of ultrasound to the distal tip member **32** and adjacent distal portion of the catheter body **26**, a flow of liquid medicament may be infused through medicament infusion side arm **98**, through the outer tube lumen **58** (outboard of the outer surface **60** of the inner tube **52**) through drug infusion passageway **70** and out of the medicament outlet apertures **68**, **69** formed at spaced locations around the outer surface of the distal catheter body **26** and distal tip member **32**. The concomitant delivery of ultrasound causes the distal member **32** and the adjacent distal portion of the catheter body **26** to vibrate in a manner which causes the medicament flowing out of apertures **68** and **69** to become thoroughly disseminated, dispersed or atomized. Additionally, the effect of the ultrasonic vibration on the adjacent vascular tissue and/or matter (e.g., thrombus) to be ablated may enhance the action of the medicament on the adjacent vascular tissue and/or matter to be ablated.

After the ablation procedure has been completed, and the desired dose of medicament has been delivered, the catheter **12** may be extracted and removed from the body.

The concurrent delivery of the medicament with ultrasonic vibration may improve the dissemination and delivery of the medicament from the catheter tip due to the physical dispersing or atomizing effect of the vibration of the catheter **12**. Also, for at least some drugs or therapeutic agents, the local absorption and/or effectiveness of the drug or therapeutic agent may be improved or enhanced by a physiological effect of the ultrasound acting on the adjacent tissue or matter being acted upon by the drug or therapeutic agent. For example, physiological effects of ultrasound on vascular tissue have been described in the following publications: Fischell, T. A., Derby, G., Tse, T. M. and Stadius, M. L.; Coronary Artery Vasoconstriction Routinely Occurs After Percutaneous Transluminal Coronary Angioplasty: A Quantitative Arteriographic Analysis; Circulation; Vol 78; 1323–1334 (1988); Chokahi, S. K., et al., ULTRASONIC ENERGY PRODUCES ENDOTHELIUM-DEPENDENT VASOMOTOR RELAXATION IN VITRO, Abstracts of the 62nd Scientific Sessions of the American Heart Association (1989).

## EXAMPLES

The following are illustrative examples of clinical situations in which the above-described ultrasound delivery/drug infusion catheter may be utilized.

### Example I

Post Infarct Ablation of a Coronary Obstruction with Concomitant Delivery of a Thrombolytic Agent

Following the diagnosis of an acute myocardial infarction in a human patient, it is determined radiographically that the left anterior descending coronary artery is significantly occluded and that blood flow to the infarcted myocardium is thereby impaired.

A coronary guide catheter is inserted, percutaneously, into the patient's femoral artery and such guide catheter is advanced to a location where the distal end of the guide catheter is in the left coronary ostium. A guide wire **40** is advanced through the lumen of the guide catheter to a location where the distal end DE of the guidewire **40** is immediately adjacent or actually passed through the obstruction within the left anterior descending coronary artery. With such positioning of the guide wire **40** may be confirmed by fluoroscopic means.

A catheter **12** of the present invention, as shown in FIGS. **1–5**, is advanced over the prepositioned guide wire **40** by inserting the exteriorized proximal end of the guide wire into the guide wire passage bore **34** formed in the distal tip **32** of the catheter **12**. The catheter **12** is advanced over the guide wire **40**, such that the proximal end of the guide wire **40** will emerge out of guide wire/coolant infusion side arm **88**. When the catheter **12** has been advanced to a point where the distal end of the catheter **12** is immediately adjacent the coronary obstruction to be ablated, the guide wire **40** may be extracted through guide wire/coolant infusion side arm **88** and removed.

Thereafter, a bag or other container of sterile 0.9 percent NaCl solution may be connected, by way of a standard solution administration tube, to the guide wire/coolant infusion side arm **88** and a slow flow of saline solution may be pumped or otherwise infused through sidearm **88**, through the inner tube lumen **64**, and out of the guide wire passage bore **34** of the catheter **12**. An intravenous infusion pump or intravenous bag compression apparatus may be utilized to provide such flow of coolant fluid through the catheter.

The proximal connector assembly **24** of the catheter **12** is connected to the ultrasound transducer **14**, and the ultrasound transducer **14** is correspondingly connected to the signal generator **16** so that, when desired, ultrasonic energy may be passed through the catheter **12**.

A 1 cc tuberculin syringe filled with room air or carbon dioxide ($CO_2$) is attached to the Luer connector **108** on the proximal end of the balloon inflation tube **74** and may be utilized to inflate and deflate the occlusion balloon **71**, as required.

An intravenous infusion bag or other container containing a prepared liquid solution of Tissue Plasminogen Activator (TPA) is connected, by way of standard intravenous infusion tubing, to medicament infusion side arm **98**. An intravenous infusion pump is coupled to the infusion tubing to permit control over the rate at which the TPA solution is infused through the catheter **12**.

When it is desired to commence the ablative procedure, the flow of coolant infusion through guide wire/coolant infusion side arm **88** is maintained at an appropriate slow flow rate while the signal generator **16** is periodically actuated/deactuated by compression/non-compression of on/off foot pedal **20**. When actuated, the electrical signals from the signal generator **16** will pass through cable **22** to ultrasound transducer **14**. Ultrasound transducer **14** converts the electrical signals into ultrasonic energy and the ultrasonic energy is passed through the ultrasound transmission member **30** of the catheter **12** to the distal end of the catheter **12**.

The catheter **12** may be manipulated back and forth by the operator to ablate the entire obstructive lesion, thereby restoring patency to the occluded coronary artery.

Before, during or after the ultrasonic ablative procedure, a prescribed amount of the TPA solution may be infused through medicament infusion side arm **98**, by actuation and adjustment of the intravenous infusion pump or other infusion system being utilized. Such will cause the TPA solution to flow, at a prescribed rate, out of the medicament outlet apertures **68**, **69** the catheter **12**. Such passage of the TPA solution out of the medicament outlet aperture **68**, **69** concurrently with the ultrasonic vibration of the distal tip **32** and distal portion of the catheter body **26** will result in vibratory dispersion or atomization of the TPA solution as it passes out of the medicament outlet aperture **68**.

During time periods when the TPA solution is being infused through the catheter **12**, it may be desirable to inflate the occlusion balloon **71** to block bloodflow through the artery while the TPA solution is being infused. It may be desirable to periodically deflate the balloon **71** to restore perfusion through the left anterior descending coronary artery or alternatively, to deliver an oxygenated perfusate as the coolant fluid being infused through the catheter **12** oxygenated perfusate will pass out of the guidewire bore to the myocardium even when the balloon **70** is inflated.

After the ultrasonic ablation procedure has been completed, and after the desired dose of TPA has been delivered through the catheter **12**, the infusion of TPA through medicament infusion side arm **98** will be ceased and the signal generator **16** will be deactuated.

The syringe mounted on the proximal end of the balloon inflation tube **74** will be checked to make certain that the balloon **70** is fully deflated, and the catheter **12** will be extracted from the coronary artery, into the guide catheter.

Thereafter, the guide catheter, with the ultrasound delivery/medicament infusion catheter **12** positioned therein, may be retracted and removed from the body.

By the above-described procedure, the ultrasound delivery/medicament infusion system **10** of the present invention has been used to remove an obstruction from the coronary artery of a post-myocardial-infarction patient, and to concomitantly deliver a desired dose of TPA to the affected myocardium so as to minimize the severity of myocardial damage which may result from the infarct, in accordance with standard thrombolytic post-infarction treatment protocols.

Example II

Treatment of a Peripheral Vascular Obstruction with Concomitant Delivery of VasoDilating Drugs

In this example, the ultrasound delivery/medicament infusion system **10** of the present invention is utilized to ablate a thrombotic obstruction in a leg artery of a human patient, and to deliver a vasodilating medication to prevent and/or treat vasoconstriction which may occur prior to, during or after the ultrasonic ablation procedure.

A guidewire **40** is initially inserted percutaneously and advanced to a location within the vasculature, adjacent the obstruction to be treated. Thereafter, the catheter **12** is advanced over the guidewire by inserting the proximal end of the guidewire into the guidewire passage bore **34** and advancing the catheter in the distal direction such that the proximal end of the guide wire enters the guide wire diverter tube **92** of the proximal connector assembly **24** of the catheter, and is diverted thereby out of guide wire/coolant infusion side arm **88**.

When the distal end of the catheter **12** has reached its desired operative position adjacent the obstruction to be treated, the guide wire **40** may be extracted and removed and a coolant solution (e.g., sterile 0.9 percent NaCl solution) may be infused through guide wire/coolant infusion side arm **88** in accordance with standard clinical solution administration procedure. The flow rate of coolant solution through the catheter **12** may be adjusted such that a constant slow infusion is maintained.

An intravenous solution bag containing a prepared solution of hydralazine (Apresolone™ Parenteral, CIBA Pharmaceutical Company, Summit, N.J.), is connected to medicament infusion side arm **98** by standard solution administration tubing and an intravenous pump is attached to the tubing to control the rate at which the hydralazine solution is infused through the catheter **12**.

A 1 cc tuberculin syringe may be inserted into the leur connector **108** on the proximal end of the balloon inflation tube **74** to permit periodic inflation/deflation of the occlusion balloon **70**.

The proximal connector assembly **24** of the catheter **12** is connected to the ultrasound transducer **14** and the signal generator **16** is periodically actuated to deliver a preset electrical signal through cable **22** to transducer **14**. Transducer **14** converts the received electrical signal to ultrasonic vibration and such ultrasonic vibration is passed through the ultrasound transmission member **30** to the distal end of the catheter **12**.

The catheter **12** may be manually manipulated back and forth such that the ultrasonic vibration of the distal tip member **32** and distal portion of the catheter body **26** will effect ultrasonic ablation of the thrombotic obstruction within the leg artery of the human patient.

Concurrently with the delivery of ultrasonic vibration through the catheter **12**, the hydralazine solution may be infused, at a prescribed rate, through medicament infusion side arm **98**, through catheter **12**, and out of medicament outflow apertures **68** and **69**. The infusion of the hydralazine solution simultaneously with the delivery of ultrasonic vibration will result in the hydralazine solution flowing out of medicament outflow apertures **68**, **69** becoming atomized or dispersed due to the vibratory movement of the distal tip member **32** and distal catheter body **26**. Also, because ultrasonic energy has been demonstrated to relax vascular smooth muscle, the concomitant delivery of the ultrasonic energy through the catheter will cause adjacent the blood vessel to remain in a relaxed state, thereby allowing the hydralazine to act on the blood vessel in the absence of significant vasoconstriction. The duration of pharmacologic effect of the hydralazine administration may help to prevent post-ablation vasoconstriction of artery after the catheter **12** has been withdrawn and removed.

During the period of time when the hydralazine solution is being infused through the catheter **12**, it may be desirable to utilize a syringe mounted on the proximal end of the balloon inflation tube **74** to inflate the occlusion balloon **71**, thereby blocking blood flow through the artery and preventing the hydralazine solution from back flowing beyond the occlusion balloon **71**.

After the ultrasonic ablation procedure has been completed and the desired dose of hydralazine has been delivered to the blood vessel, the syringe on the proximal end of the balloon inflation tube **74** will be checked to make certain that the balloon **71** is fully deflated and the catheter **12** may be withdrawn and removed.

Although the invention has been described hereabove with respect to certain presently preferred embodiments, it will be appreciated that various changes, modifications, deletions and alterations may be made to such above-described embodiments without departing from the spirit and scope of the invention. Accordingly, it is intended that all such changes, modifications, additions and deletions be incorporated into the scope of the following claims.

What is claimed is:

**1**. A method for ultrasonic ablation of matter from an anatomical passageway of a mammalian body and for concomitant delivery of a liquid medicament, said method comprising the steps of:

inserting into the mammalian body distal end first an ultrasound delivery/medicament infusion catheter comprising an elongate flexible catheter body having a longitudinal axis, a proximal end and a distal end, a distal tip member attached to the distal end of the catheter body, an ultrasound transmission member extending longitudinally through said catheter body and attached at the distal end thereof to the distal tip member for transmitting ultrasound energy to the distal tip member, a medicament infusion lumen extending longitudinally through said catheter body and opening through at least one medicament outlet aperture formed in the distal tip member and oriented radially outward in relation to the longitudinal axis of said catheter body;

advancing the distal end of said catheter to a desired operative position relative to the obstruction to be ablated;

generating ultrasonic energy at a location outside the catheter body;

coupling said generated ultrasonic energy to the ultrasound transmission member at the proximal end of the catheter body;

passing ultrasonic energy through said ultrasound transmission member to the distal tip member at the distal end of said catheter such that the distal end of said catheter will undergo ultrasonic vibration at a frequency which will result in ablation of said obstruction; and

passing a flow of medicament through said medicament infusion lumen and out of said radially-oriented medicament outlet aperture formed in the distal tip member concurrently with the delivery of said ultrasonic energy through said catheter.

**2**. The method of claim **1** wherein the step of passing a flow of medicament further comprises:

delivering a thrombolytic agent through said catheter.

**3**. The method of claim **2** wherein said thrombolytic agent is selected from the group consisting of:

streptokinase;

urokinase;

tissue plasminogen activator; and

possible combinations thereof.

**4**. The method of claim **1** wherein the step of passing a flow of medicament comprises:

delivering an anticoagulant agent through said catheter.

**5**. The method of claim **4** wherein said anticoagulant agent is heparin.

**6**. A method for ultrasonic ablation of matter from an anatomical passageway of a mammalian body and for concomitant delivery of a liquid medicament, said method comprising the steps of:

inserting into the mammalian body distal end first an ultrasound delivery/medicament infusion catheter comprising an elongate flexible catheter body having a longitudinal axis, a proximal end and a distal end, a distal tip member attached to the distal end of the catheter body, an ultrasound transmission member extending longitudinally through said catheter body and attached at the distal end thereof to the distal tip member for transmitting ultrasound energy to the distal tip member, a medicament infusion lumen extending longitudinally through said catheter body and opening through at least one medicament outlet aperture formed in the distal tip member and oriented radially outward in relation to the longitudinal axis of said catheter body;



advancing the distal end of said catheter to a desired operative position relative to the obstruction be ablated;

generating ultrasonic energy at a location outside the catheter body;

coupling said generated ultrasonic energy to the ultrasound transmission member at the proximal end of the catheter body;

passing a flow of medicament through said medicament infusion lumen and out of said radially-oriented medicament outlet aperture formed in the distal tip member; and

passing sufficient ultrasonic energy through said ultrasound transmission member to the distal tip member at the distal end of said catheter concurrently with the delivery of said medicament through said catheter such that the distal end of said catheter will undergo ultrasonic vibration at a frequency that will result in ablation of said obstruction and that will result in the thorough dissemination of said medicament.

**7**. The method of claim **6** wherein the step of passing ultrasonic energy through said ultrasound transmission member comprises passing sufficient ultrasonic energy to the distal tip member at the distal end of said catheter such that the medicament effectiveness upon adjacent tissue acted upon by the ultrasonic energy is improved.

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